

Effect of ambient temperature on incidence of tuberculosis and effect modification by meteorological factors in Jinan, China during 2012-2015

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Abstract

Objective

For assessing the nonlinearity and delayed effect of temperature on incidence of Tuberculosis (TB) and effect modification by meteorology factors, daily data on meteorological factors, air pollutants and incidence were obtained in Jinan, China, from 2012 to 2015.

Methods

A distributed lag non-linear model (DLNM) combined with quasi-Poisson regression model was employed to assess the nonlinearity and the delayed effect of associations. We further built a series of weather-stratified models categorizing the meteorology factors into two levels to assess the effect modification of the ambient temperature effect.

Results

The correlation between tuberculosis (TB) cases and daily average temperature (T_{mean}) was nonlinear with a delayed effect. At the current day (lag 0), the increase of T_{mean} decreased the risk of TB incidence; over lag 0-70 days, the decrease of low T_{mean} and the increase of the high T_{mean} both indicated the increased risk of TB. The cold temperature showed an immediate effect at the current day, with a harvesting effect in the following days. There was no significant harvesting effect in hot effect. Meanwhile, the effect of hot temperature on TB appeared with an about two-week lag and was lower than cold effect. The effect modifications by relative humidity, wind speed and sunshine duration were observed.

Conclusion

Results indicate that there was a nonlinear correlation with a harvesting effect between temperature and TB in Jinan, and both cold effect and heat effect exist the delayed effect. Results also pointed to the importance of considering effect modification by meteorological factors in assessing temperature effects on incidence of TB. Which might shed light on the strategy of TB prevention and control.

1. Introduction

In the past decades, the prospect of continued global warming, climate change, serious pollution and extreme weather events has concentrated attention on the harmful impacts of environment on public health. Many studies [1–3] have reported an increased mortality caused by high or low temperature. However, previous studies mainly focused on the relationships between meteorological factors and chronic diseases, such as respiratory diseases (RD) [4], cardiovascular diseases (CVD) and myocardial infarction [5]. With growing concerns about climate change, an increasing number of studies also began to focus on associations of weather variability with the fluctuations of infectious diseases and suggested

that weather factors play an important role in infection incidences [6], such as hand-foot-mouth disease [7], Zika virus infection [8] and diarrhea [9].

Worldwide, Tuberculosis (TB) is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS). Millions of people continue to fall sick with TB each year. Two thirds of cases were in eight countries with the highest rates in India (27%), China (9%) and Indonesia (8%). China is not only the second largest country with the highest number of cases, but also one of the three countries with the largest numbers of multidrug-resistant and rifampicin-resistance (MDR/RR-TB) (13%). [10] TB remains an ongoing intractable health challenge in China.

TB spread pattern is influenced by geographic and social factors, which indicated it is necessary to assess the impacts of temperature on TB in various regions. Seasonal fluctuations in TB notifications have been reported from a number of researches [11–13], these studies also suggest delayed effects of environmental factors. Further, it has been shown that the risk of TB has a correlation with climate and extreme heat or cold temperatures. [14, 15] Due to the diversity of temperature ranges and fluctuations, climate types, and economic environments in different regions, the relationships between temperature and TB in different regions should be studied and will provide important evidence also for other countries.

Moreover, a lot of studies in different regions put forward that other environmental factors can also exert an effect on TB incidence. For example, the areas with extra dry climate are high-risk regions of TB [14]; the decrease of SD lead to an increased risk of TB [16]; the TB incidence are positively associated with the WS[17, 18]. The meteorological and environmental factors are some of the central variables affecting the airborne transmission of pathogens. [19, 20] Yet there have been only limited studies on effect modification by other meteorological factors on temperature effect on TB.

In addition to meteorological factors, air pollution has also been linked to TB risk. The effects of carbon monoxide (CO) and particulate matter less than 2.5 μm in aerodynamic diameter ($\text{PM}_{2.5}$) on incidence of TB were significant. [21–23] In South Korea, the exposure to high concentrations of suspended particles increased at 1.27 times the incidence of TB [24]. However, many studies [4, 14] of ambient temperature and health outcome did not account for air pollutants, and in the previous review [25], it was not clear from the few studies conducted whether air pollutants acted as confounders, effect modifiers, or both. It is critical to control the effect of pollutants in models with ambient temperature, since they may often exert the influence on a daily basis [26]. On the other hand, Jinan is a typical heavily polluted area, and the relationship between cases of TB and pollutants have been determined in Jinan. Thus, the actual association between ambient temperature and incidence can be observed, only after controlling pollutants in the models.

Here, this study aimed to assess the effect of ambient temperature as well as delayed effect on TB based on the infectious disease surveillance data in Jinan by using distributed lag non-linear model (DLNM) controlling the effects of the pollutants affecting the infection of TB. Although almost all studies that examine the effects of air pollution and mortality have controlled for meteorological factors, control for

air pollution in studies assessing the effects of temperature has been rare. Simultaneously, based on the relationship between T_{mean} and incidence of TB, this study also investigated if the other meteorological factors modify the temperature-TB incidence relationship. It will help plan effective intervention strategies for the prevention and control of TB in similar populations and help public health professionals to make response.

2. Materials And Methods

2.1 Study area and population

Jinan is located in the Mideast of China (36°01'N to 37°32'N, 116°11'E to 117°44'E). It towards the south is Tai Mountain, whilst the north is bordered by the Yellow River. Belonged to the warm temperate continental climate, four seasons. It is dry and rainless in spring, hot and rainy in summer, cool and sunny in the fall, freezing and dry in winter. As the capital city of Shandong province, Jinan is the center of politics, economies and communication in the province. The total area is 7,998 km², and the total population reaches 7.32 million. The male/female ratio of target population is 0.984. Fourteen percent of the total population is the elderly (≥ 65 years of age). In 2017, the density of population is 805 person/km². [27] In recent years, Jinan's annual average temperature has gradually increased and extreme weather events have occurred frequently with extreme T_{max} recorded 41.7 °C and extreme T_{min} recorded - 17 °C [28]. In 2017, the number of high temperature (daily maximum temperature ≥ 35 °C) days reached 30, which was the most numerous days for nearly two decades. [29] At the same time, Jinan is a typical high-pollution city. At the beginning and end of each year, continuous haze appears in Jinan. [29, 30]

2.2 Data collection

Daily TB cases counts data, from January 1, 2012 to December 31, 2015, were obtained from Jinan Municipal Center for Disease Control and Prevention (JMCDC), which has access to the China National Notifiable Disease Surveillance System. As a notifiable infectious disease in China, all cases of TB are required to be reported online within 24 hours after diagnosis in the hospital. The TB cases in the JMCDC database included all newly diagnosed active pulmonary TB cases.

Daily meteorological data including daily maximum (T_{max}), mean (T_{mean}), and minimum (T_{min}) temperature, mean relative humidity (RH), wind speed (WS), sunshine duration (SD), air pressure (PRESS) and daily amount of precipitation (PRCP) were collected from the China Meteorological Sharing Service System Network (<http://cdc.cma.gov.cn/home.do>) during the same period as the TB cases data.

Daily mean hourly air pollutants data (inhalable PM_{2.5} and CO) were obtained from the Jinan Environmental Monitoring Center. The data was obtained from 14 fixed monitoring stations, spanning the entire region, including 11 sites located in urban areas and 3 sites located in suburban county areas.

Daily average values of air pollution were used in this study and calculated the average from above 14 fixed monitoring stations.

2.3 Statistical analysis

Firstly, a descriptive analysis was performed to describe the distribution of TB cases, meteorological factors and pollutants during the study period. The minimum, maximum, quartiles, mean and standard deviation were calculated. The associations of TB cases with meteorological factors and air pollutants were assessed by Pearson's correlation test. Factors related to the incidence of TB were included in the model.

Secondly, the effect of T_{mean} on TB cases was estimated utilizing a distributed lag non-linear model (DLNM) with quasi-Poisson regression. DLNM, a flexible modelling framework, describes simultaneously the shape of the relationship along both the space of the predictor and the lag dimension of its occurrence. [31]. As potential confounders, long-term trend/seasonality (by using day of study), day of the week (DOW), public holiday (HOD), RH, WS, SD, CO and $\text{PM}_{2.5}$ were considered. Their effects were removed on by using smooth functions to calculate net effect of T_{mean} on incidence of TB. [32] The degrees of freedom (df) of splines in different functions were automatically selected by Generalized Approximate Cross-Validation (GACV). The Pearson's correlation test and collinearity diagnosis were used to analyze the correlation and collinearity between the various factors. Generally, when $|r_s| \geq 0.8$, it is considered that there is a strong correlation between factors; when the variance inflation factor (VIF) ≥ 10 , it is considered that there may be a serious collinearity between factors [33, 34].

Instead of using a linear term, a cross matrix for the daily temperature was established to represent the non-linear and delayed effect. We selected a natural cubic spline basis to model the non-linear effects using three df in the temperature space, and the polynomials with four degrees to examine the delayed effect. Model selection for lag structure was carried out by minimizing the GACV criteria; these lag structure (3, 4, 5, 6, 7, 8, 9, 10, 11, 12 weeks) corresponded to different GACV values (1.680, 1.677, 1.680, 1.667, 1.666, 1.673, 1.665, 1.655, 1.661, 1.661) during the modeling attempt. Referring to the previous study [14, 35] and GACV values, we set a maximum lag structure as 70 days (10 weeks) as it also is longer than the incubation period (4-8weeks). We used a temperature of 15.0 °C (which was mean value of the T_{mean} in Jinan, 2012 to 2015) as the reference value to calculate the relative risks (RRs), and used the minimum, the 5th and 25th of percentiles temperature as the cold temperature effect and the maximum, the 95th and 75th of percentiles temperature as the hot temperature effect.

Thirdly, a weather-stratified DLNM was developed to quantify the effect modification by other meteorological factors (RH, WS and SD). We used this model to estimate the temperature effect for two meteorological factors strata: <50th percentile and > 50th percentile. Meanwhile, in the research process, it was found that the effects of temperature ranging from the 25th to 75th quantile were basically not significant. We selected a double threshold function as basis to model the cold and hot temperature effects with the 25th and 75th quartiles as the cut-off points. We used the interval as a reference to estimate the cold temperature effect (the 5th percentile) and hot temperature effect (the 95th percentiles)

by the RR with 95% CI. Further, we also insert an interaction function of T_{mean} with RH, WS or SD to identify whether the exists of effect modifications are due to chance. [36]

2.4 Sensitivity analyses

To check the robustness and validity of the main findings of this study, sensitivity analyses were performed by adjusting df of temperature (df = 2,4,5), fitting the models to TB cases at lag 0 and lag 0–70 days. Further, we also conducted sensitivity analyses by adjusting one environmental factor at a time or excluding all air pollution factors ($\text{PM}_{2.5}$, CO) or all meteorological factors (RH, WS, SD) from the model.

In this study, the relative risk (RR) and 95% confidence interval (95% CI) were used as the evaluation indexes of the effect. The analysis was performed by Stata software (version 15.0) and packages (splines, DLNM, mgcv) of R statistical software (version 3.5.2). Statistical significance was set at $P < 0.05$.

3. Results

2.5 Descriptive analysis

During the study period January 1, 2012 to December 31, 2015, 15,010 cases of TB were notified in the study area, and average T_{max} was 19.9°C, T_{mean} 15.0°C, T_{min} 10.8°C in Jinan. The 5th, 25th, 75th and 95th percentiles of daily T_{mean} were - 1.8°C, 5.2°C, 24.0°C and 29.0°C. Table 1 presents descriptive statistics for TB cases, pollutants and meteorological factors in Jinan, respectively. The mean concentrations of $\text{PM}_{2.5}$ and CO were 97 $\mu\text{g}/\text{m}^3$ and 1408 $\mu\text{g}/\text{m}^3$. The time-series distributions of TB cases and meteorological factors were shown in Fig. 1, demonstrating a seasonal trend for the series. The minimum of T_{mean} gradually increased from 2012 to 2015, and the cases of TB fluctuated slightly with more cases occurring in spring and fall.

Table 1

Summary of daily environmental variables and incidence of TB in Jinan city, 2012–2015

Variables	Minimum	Percentile			Maximum	
		25th	50th	75th		
Pollutants ($\mu\text{g}/\text{m}^3$)						
PM _{2.5}	15	59	83	118	443	97 ± 58
CO	465	990	1238	1631	6555	1408 ± 654
Meteorological Factor						
Daily T _{mean} (°C)	-9.4	5.2	16.9	24.0	33.8	15.0 ± 10.5
Daily T _{max} (°C)	-5.4	9.7	22.3	29.4	39.9	19.9 ± 10.9
Daily T _{min} (°C)	-12.9	1.3	12.2	20.0	30.8	10.8 ± 10.3
Daily RH (%)	14	41	55	70	100	56 ± 20
Daily SD (h)	0.00	3.20	7.00	9.00	13.30	6.15 ± 3.73
Daily WS (m/s)	0.2	1.8	2.3	3.0	8.4	2.5 ± 1.1
Daily PRESS (hPa)	975.7	988.7	996.7	1003.6	1021.8	996.5 ± 9.1
Daily PRCP (mm)	0.00	0.00	0.00	0.00	600.00	4.43 ± 26.90
Case						
TB	0	2	4	7	26	5 ± 4
PM _{2.5} fine particulate matter with an aerodynamic diameter of < 2.5 μm , CO carbon monoxide, T _{mean} daily average temperature, T _{max} daily maximum temperature, T _{min} daily minimum temperature, RH relative humidity, SD sunshine duration, WS wind speed, PRESS pressure, PRCP daily amount of precipitation, TB case of TB						

2.6 Correlation analysis and collinearity diagnosis between TB cases and environmental factors

Table.S1 exhibits the matrix of Pearson correlations between TB cases and other variables. TB was positive correlated with T_{mean}, T_{max}, T_{min}, SD and WS, and negative correlated with PM_{2.5}, CO, PRESS and RH (P < 0.05). No statistical association was found between the TB cases and PRCP (P > 0.05). However, there was a strong negative correlation between PRESS and T_{mean} ($r_s = -0.87$), and hence collinearity might exist. Variable PRCP unrelated to the number of cases and variable PRESS strongly related to

T_{mean} were excluded from the model, and other meteorological factors were included in. Through collinearity diagnosis, it was found that the VIF values of all factors in the model were ≤ 5 , so there was no severe collinearity, and the model was established.

2.7 The relationships between T_{mean} and number of TB cases

Figure 2 illustrates the three-dimensional graph of a nonlinear relationship between T_{mean} and TB cases, with reference at 15.0°C. An immediate effect of the minimum temperature was observed on the current day (lag 0), with lower risk in the following days. Figure 3 presents the lag-response relationships between different T_{mean} levels (minimum, the 5th, 25th, 75th and 95th percentiles and maximum temperature) and incidence. The effect of the minimum temperature (-9.4 °C) led to the risk in TB incidence at lag 0 and the second incidence peak at the lag 57. It also showed the decrease trend of the risk and the lowest effect occurred at lag 23 (RR = 0.95, 95% CI: 0.93, 0.97). The effect of the 5th percentile of T_{mean} (-1.8 °C) also presented a similar trend. The effect of the 25th percentile of T_{mean} (5.2 °C) remained insignificant and the risk of the 75th percentile (24.0 °C) fluctuated slightly. Meanwhile, the 95th percentile (29.0 °C) peaked after lag 14 and had no significance in the following days. For maximum T_{mean} (33.8 °C), we found a consistent increase risk until the incidence peak at lag 16.

The lag effect and cumulative effect of temperature on TB incidence after different lag days when controlling for long-term trends, HOD, DOW, and meteorological factors and air pollution are shown in Fig. 4. Low temperature increased the relative risk of TB incidence at the lag 0. The overall cumulative effect showed a U-shape; however, effects had considerable statistical variability reflected by large confidence intervals due to a small number of maximum and minimum T_{mean} days. More specifically, relative to 15.0 °C, the colder temperature showed a lower risk after lag 21 and lag 0–42 days. After lag 63, the risk of TB incidence increased with the decrease of T_{mean} , and the cumulative risk of 10.1 °C was 0.90 (95% CI: 0.81, 1.00) and of 25.2 °C was 1.18 (95% CI: 1.02, 1.37) after lag 0–63 days.

2.8 The effect modification by meteorological factors

Combined the effects at the cold temperature (the 5th percentile of T_{mean} : -1.8 °C) compared with the 25th percentile (5.2 °C) and the hot temperature (the 95th percentile of T_{mean} : 29.0 °C) compared with the 75th percentile (24.0 °C), are presented in Fig. 5. High RH increased the risk of TB in hot temperature situation after lag 21 and in cold temperature situation after lag 70, respectively; meanwhile, low RH decreased the risk of TB in cold temperature situation after lag 21 and in hot temperature situation after lag 70. In addition, low WS increased the risk for different temperature at different lag period; and high WS decreased the risk in hot temperature at lag 49. Furthermore, low SD increased the risk in cold temperature situation at lag 21. By verifying the interaction terms, the interactions of RH ($P = 0.001$), WS ($P = 0.004$) and SD ($P = 0.02$) with T_{mean} were significant, respectively.

2.9 Sensitivity analyses

Table.S2 contains details of the results from the sensitivity analyses. When we changed df (2, 4, 5 df) for the temperature space in the DLNM, the estimated changes were slightly smaller. Adjusting for meteorological factors slightly changed the overall cumulative RRs, whereas adjusting for air pollution gave slightly larger in cold effect but still did not change substantially. Our sensitivity analyses suggested that the results were not dependent on modeling assumptions.

4. Discussion

We examined the effects of ambient temperature on TB cases in Jinan, one of the so-called four “ovens” with serious air pollution in mid-eastern China, during the period of 2012 to 2015. Study findings indicated that the temperature–incidence relationship was non-linear, with showing an S-shape at the current day and a U curve over lag 0–70 days. Further, the minimum T_{mean} effect appeared immediately with a following harvest effect, and the second onset peak appeared after lag 8–9 weeks, whereas the maximum T_{mean} effect became predominant with about two weeks’ lag. Meanwhile, the T_{mean} effect on incidence of TB modified by different levels of RH, WS and SD, and varied across different lag period.

Our results of a negative and non-linear relationship between ambient temperature and notified cases of TB infection are consistent with research carried out in other countries with different weather conditions [14, 17, 35]. We also found that the risk of TB incidence was greatly affected by extreme temperature on the current day. On the other hand, the overall cumulative effect showed trends for increased risks for decline of cold temperature and increase of hot temperature.

Many investigators [14, 17, 37] have reported the delayed effect in the relationship between TB and cold or hot effect. Our study also confirmed that the delayed effect existed. For the effects of the minimum and the 5th percentile of T_{mean} , the immediate effects appeared at that day, and the second onset peak appeared at lag 8–9 weeks. For the effects of the 75th, 95th percentiles and maximum of T_{mean} , the onset peak appeared after lag about two weeks. The peak of cold effect appeared earlier than that of hot effect, which is comparable to the results of a study [14] conducted in Japan. In contrast to this study’s findings, however, the results in the Japan study showed that high temperature effects were generally constant at lag periods of up to 12 weeks, whereas the effects in low temperature ranges were persistent over shorter lag periods and diminished over time. This may be due to the warm climate in Japan, so the 5th percentile temperature (5.4 °C) in the Japan study was only equivalent to the 25th percentile in our study. Yuanyuan Xiao[35] found that average temperature was inversely associated with TB incidence at a lag period of 2 months. Similarly, we found that T_{mean} under 15 °C was also negatively associated with TB at lag 63, but hot effect was not significant.

The difference in lag effects as our results of DLNMs suggested would be also related to some characteristics, and some researchers have provided this context for interpreting our results. Fares [38] manifested that lower temperature during winter may induce the susceptibility to respiratory epithelium infection. The fluctuation in weather temperature during winter may also act on the respiratory epithelium by slowing mucociliary clearance and inhibiting phagocytosis, causing pathophysiological responses,

which then lead to increase the susceptibility to infection. [39] In addition, in winter in Jinan, the citywide coal-burning heating exacerbates smog, which would increase the number of carriers that can spread pathogens [20] and increase the risk of RD; Liu [23] provided the evidence that heavy pollution are positively correlated with TB incidence. Furthermore, Naranbat [13] hypothesized that temperature may change the time people spend at home or outside. China is a populous country, people gather, and close door and windows during the cold winter, and the crowded indoor environment is also a risk factor for infectious diseases. As the temperature gradually increases with an agreeable weather, citizens were more willing to play outside and open the window for ventilation. Meanwhile, the heat of the summer might trigger a thermal reaction, but it also comes with a reluctance to congregate for residents, preferring to stay indoors with air conditioning. Which may not induce the high risk of transmission of tuberculosis as cold temperature do.

We found some evidence of harvesting effect in our study; there was an incidence deficit for the minimum and the 5th percentile T_{mean} at the lag about 3 weeks. We speculate that the harvesting effect would support the mechanism of temperature influencing the incidence risk. In particular, it may be that presents in extreme cold temperature only hasten the TB incidences of individuals in a small, frail, infected subset of the population who will attack even in the absence of extreme cold effect. A possible reason is extreme cold air attacks the body's respiratory and immune systems, speeding up the onset of TB to infected people. In contrast, hot temperature might mainly disturb the body's cardiovascular system, and has little direct effect on the respiratory system. [40]

However, meteorological factors may play an important role. Our findings showed that low RH decreased the risk of TB for temperature which was different from Yingjie Zhang's research[41]. In cold temperature situation, the increased RH may create a suitable environment for the growth and reproduction of tuberculosis. Our study also suggested that low WS could increase the effect of low T_{mean} on TB at the current day and at lag 70. The higher WS could accelerate ventilation, dilute the concentration of bacteria and help reduce the risk of becoming infected. Although another study [18] indicated that areas with stronger wind speeds tend to have a higher infection risk, our study findings were supported by the findings of Kai Cao[42]. As has been found in a few other studies [17, 42, 43], the low SD would raise the risk of TB. Our findings showed that the low level of SD positively modified on cold temperature effect. We speculate that this result would be also related to some view point indicated by these studies [44, 45] on TB that low serum vitamin D levels were associated with higher risk of active tuberculosis. The low SD would affect the absorption of vitamin D for public. However, there was still a lack of validation of biological mechanisms of vitamin D on TB, which should be a further direction.

A study limitation is the use of data on temperature and air pollution from fixed monitoring sites rather than measuring individual exposure, which would bring about measurement errors because individual exposure temperature may be not entirely identify with outdoor average temperature. Secondly, cold effect and hot effect was calculated by comparing the 5th to the 25th percentile and the 95th to the 75th percentile temperatures. This accounted for the effect of cold and hot temperature to some extent. But the reason for this way is that the study population is not sensitive to T_{mean} ranging from the 25th to the

75th percentile, there may be inappropriateness when extrapolating calculating method to an unequal population or other diseases. Because the complexity of other factors and the difference of population adaptation. In addition, we only used data from Jinan to examine the effects of temperature on incidence of TB so the findings may not be generalizable to other areas.

In conclusion, tuberculosis incidence in Jinan was found to be nonlinear and negative related with temperature, with a harvesting effect for cold temperature. Findings of this study add to the evidence that high temperatures have slower delayed effects on TB incidence while low temperatures appear to exhibit higher effects. Temperature may determine the amount of time spent indoors and affect the ability of bacteria to survive, and thus the transmissibility of *Mycobacterium tuberculosis*. Results also suggest that considering effect modification by RH, WS and SD in assessing temperature effects on TB incidence may be essential. These findings may have important implications for public health officials to control and prevent the TB risk of exposure to ambient temperature. Meanwhile, the public are also suggested to keep clear life environment, ventilate usually and supplement Vitamin D. Although China has achieved the 2015 global TB control goal, still a million incident TB cases are reported annually. [10] Exploring the influencing factor and mechanism of TB can shed light on future TB control programs in China and even other country.

5. Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

RY process the conceptualization and formal analysis by software and writing of original draft; LC process the investigation and collect the data, funding acquisition and supervision for study; RY and LC contributed equally to this work and should be considered as co-first authors; JZ and MW process the investigation for this research and funding Acquisition; CJ process the conceptualization and methodology for the research design and formal analysis; SR process the visualization and funding acquisition for this study; CJ and SR contributed equally should be considered as co-corresponding authors. All authors read and approved the final manuscript.

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Supplementary Files Legend

Table. A.1 Pearson correlations between meteorological factors, air pollutants and incidence of TB in Jinan city, 2012-2015

Table. A.2 Sensitivity analyses of estimating association of temperature with TB incidence at lag 0 and over lag 0-70 days by changing degrees of freedom (df) and confounders in modeling assumptions

Figures

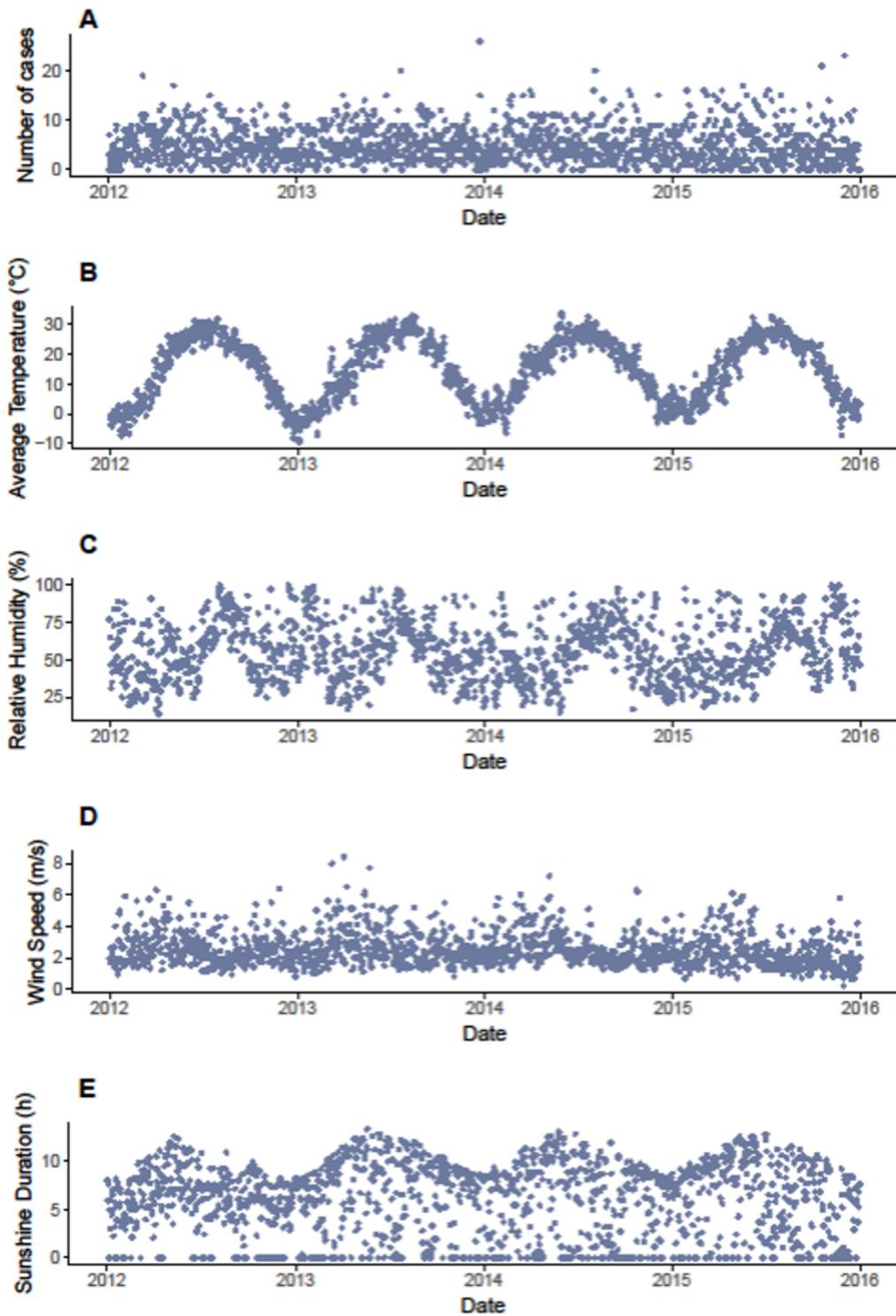


Figure 2

Daily time series of number of tuberculosis cases and meteorological factors for the period from 2012 to 2015 in Jinan

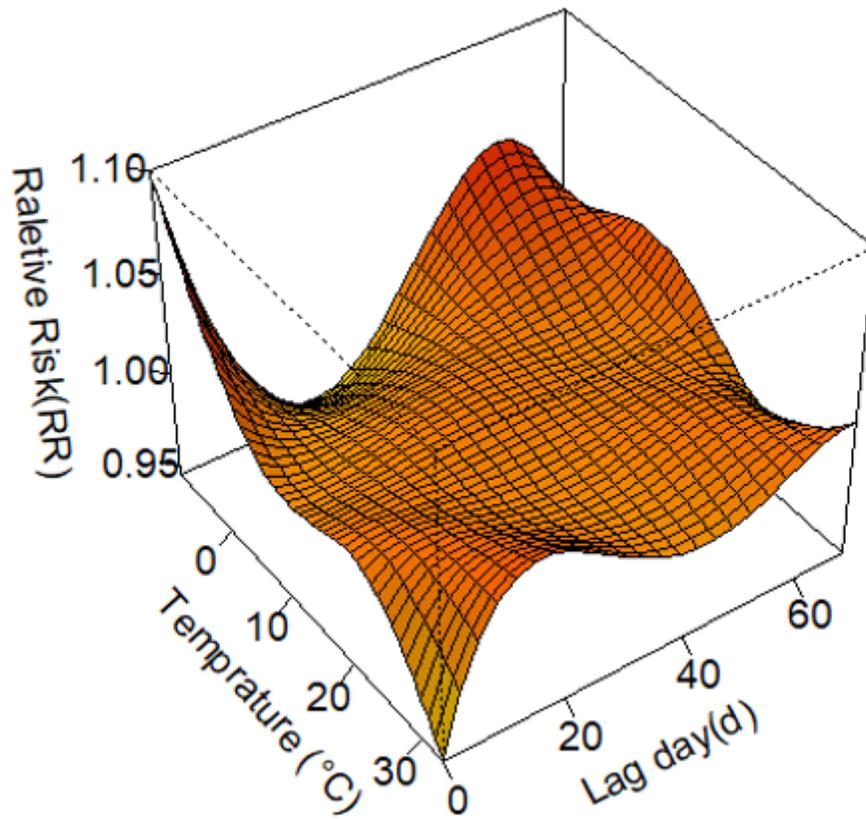


Figure 3

Relative risk of incidence of tuberculosis by daily average temperature (°C) and days of lag, with reference value at mean temperature (15.0 °C), adjusting for PM2.5, CO, relative humidity, wind speed, sunshine duration, public holiday, day of the week, and time trend

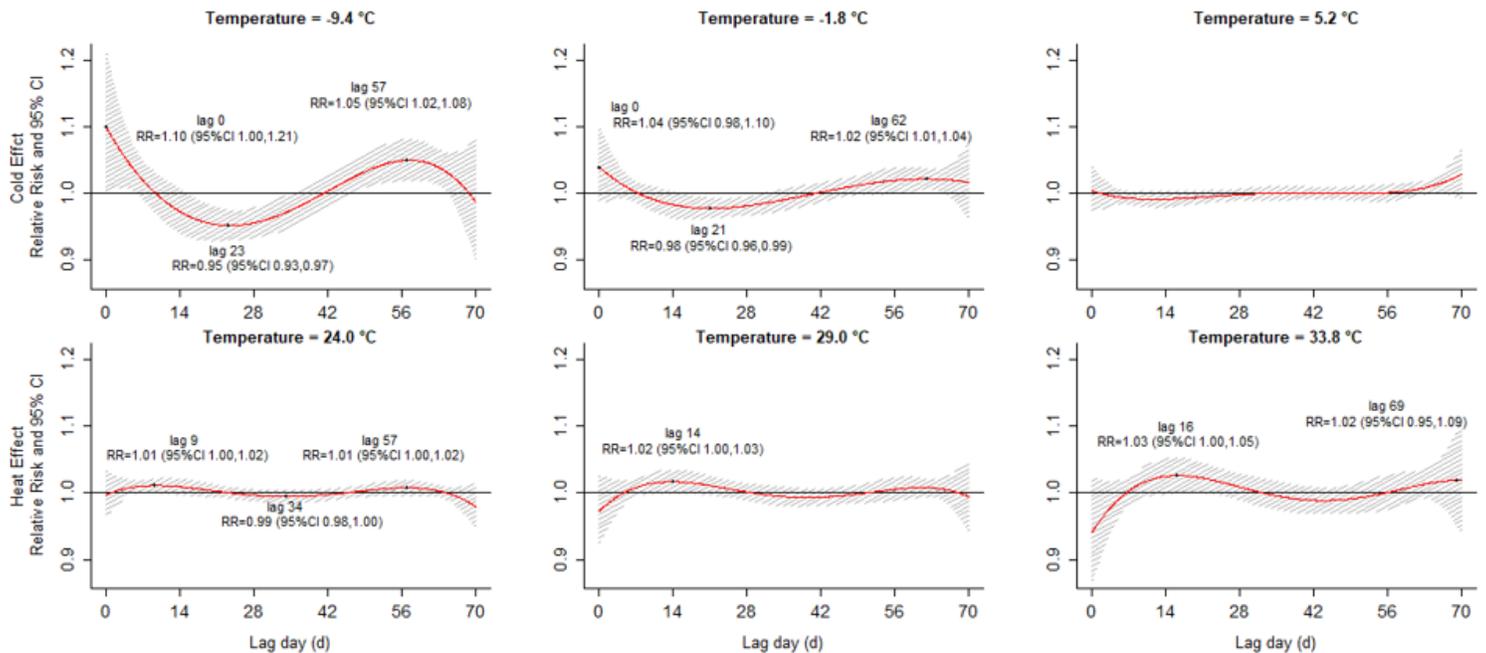


Figure 5

The effects of daily average temperature (°C) on incidence of tuberculosis along days of lag, adjusting for PM2.5, CO, relative humidity, wind speed, sunshine duration, public holiday, day of the week, and time trend. The continuous curves are relative risks of incidence comparing the minimum, 5th, 25th, 75th, 95th and maximum percentile of temperatures with 95% CI (shaded area)

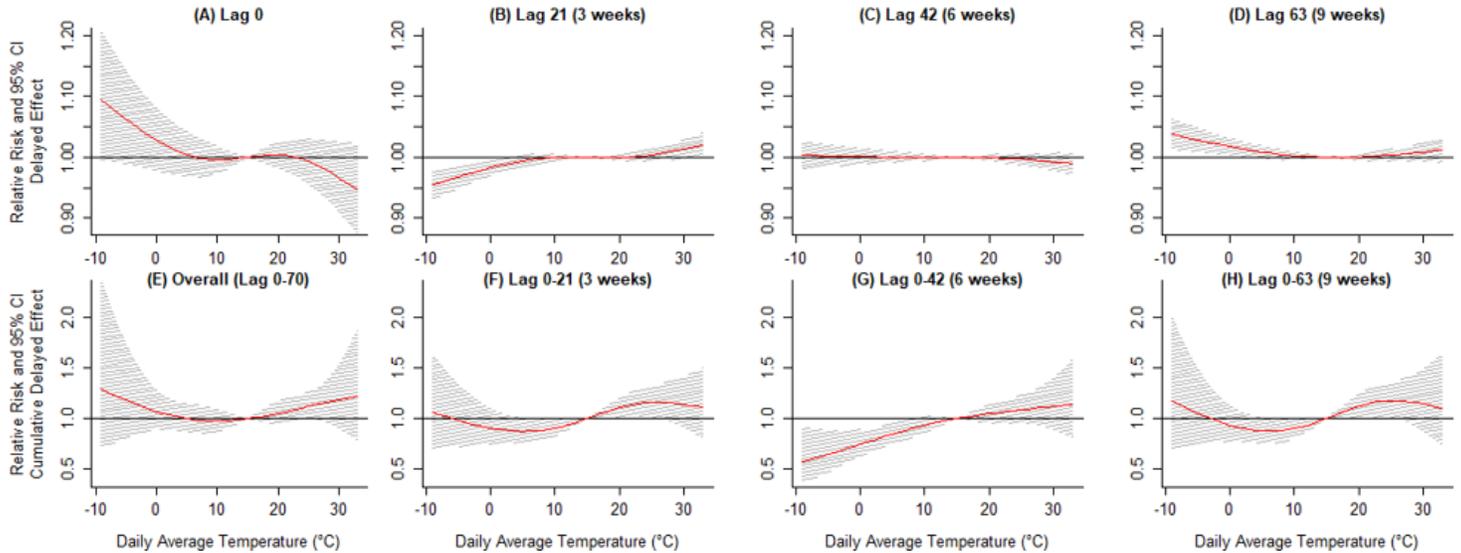


Figure 7

Pooled relative risks of TB incidence by daily average temperature over (A)lag 0, (B)lag 21, (C)lag 42, (D)lag 63, (E)lag 0-70, (F)lag 0-21, (G)lag 0-42, (H)lag 0-63 days, adjusting for PM2.5, CO, relative humidity, wind speed, sunshine duration, public holiday, day of the week, and time trend. The continuous curves represent the RRs for incidence with reference at 15.0 °C, with the 95% CI (shaded area)

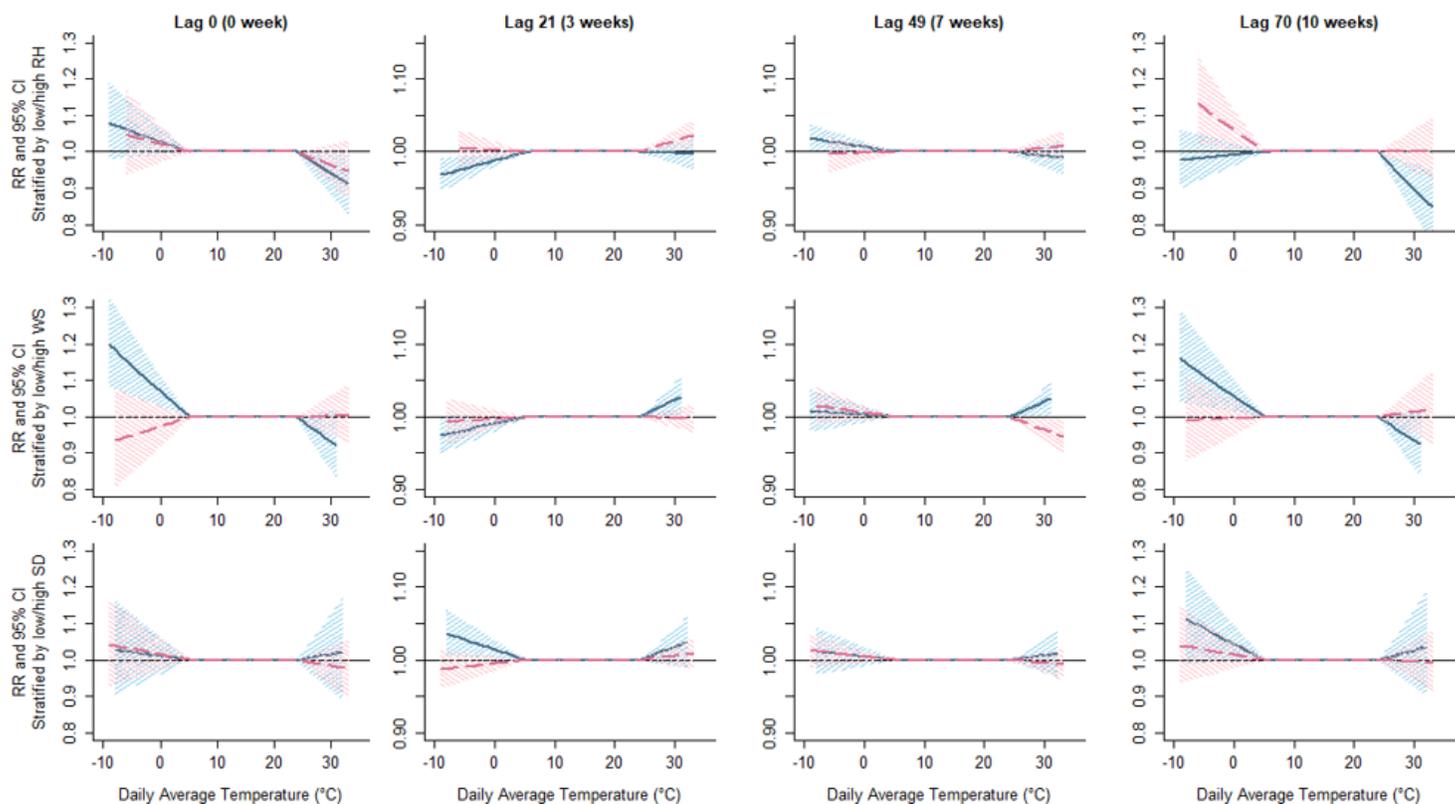


Figure 10

Effect modification of the association between daily average temperature ($^{\circ}\text{C}$) and tuberculosis by relative humidity (RH), wind speed (WS) and sunshine duration (SD) strata, adjusting for PM_{2.5}, CO, public holiday, day of the week, time trend and other meteorological factors. The solid lines are the RRs of temperature for the low level strata, while the dotted lines are the RRs of temperature for the high level strata, with the 95% CI (shaded area)

Supplementary Files

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